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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/423,109	10/29/1999	Jacques Paris	GEI-073	6348

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DENNISON, SCHULTZ & MACDONALD
1727 KING STREET
SUITE 105
ALEXANDRIA, VA 22314

EXAMINER	
QAZI, SABIHA NAIM	
ART UNIT	PAPER NUMBER
1612	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/423,109	PARIS ET AL.	
	Examiner	Art Unit	
	Sabiha Qazi	1612	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on _____.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3,4,7,8,18,31 and 33-37* is/are pending in the application.

4a) Of the above claim(s) *33-37* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3,4,7,8,18 and 31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *33-37* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Final Office Action

Claims 3, 4, 7, 8, 18, 31 and 33-37 are pending. Claim 33-37 are withdrawn from consideration as non-elected invention. Amendments are entered. No claim is allowed.

Summary of this Office Action dated Saturday, November 22, 2008

1. Priority
2. Information Disclosure Statement
3. Copending Applications
4. Specification
5. Double Patenting Rejection
6. 35 USC § 103(a) Obviousness Rejection – First Rejection
7. 35 USC § 103(a) Obviousness Rejection – Second Rejection
8. Response to Remarks and Declaration
9. Conclusion
10. Communication

Priority

Specification should contain the priority data of the application. This application is 371 of PCT/FR99/02588 (10/25/1999).

Information Disclosure Statement

The IDS is enclosed with this action. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609.04(a) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Copending Applications

Applicants must bring to the attention of the examiner, or other Office official involved with the examination of a particular application, information within their knowledge as to other **copending United States applications**, which are "material to patentability" of the application in question. MPEP

2001.06(b). See Dayco Products Inc. v. Total Containment Inc., 66 USPQ2d 1801 (CA FC 2003).

Specification

The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Double Patenting Rejection

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s).

See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

1. Claims 3, 4, 7, 8, 18, 31 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-6

of U.S. Patent No. 6,831,073. Although the conflicting claims are not identical, they are not patentably distinct from each other because presently claimed invention is considered obvious over claims 1-6 of US '073.

2. Instant claims differ from the reference in claiming "a method of treating menopausal women" wherein the claims of issued patent cites "a method of treating estrogenic deficiencies" and "avoiding the appearance of osteoporosis" which are considered obvious. Treatment of menopausal women includes treating estrogenic deficiency or treating osteoporosis.

3. It would have been obvious to one skilled in the art to prepare addition beneficial composition useful for avoiding osteoporosis and to treat estrogenic deficiencies. Motivation has been provided in the claims and also in the specification. One who is familiar with the art would have been motivated to prepare compositions of estradiol ester such as the combination of estradiol valerate and nomegesterol acetate (NOMAC) and use for the treatment of estrogen deficiencies and to avoid osteoporosis. The amounts and dosage are the same as in issued patent. The effect of this combination is considered inherent.

Claim Rejections - 35 USC § 103—1st Rejection

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be *obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patent ability shall not be negatived by the manner in which the invention was made.*

This application currently names joint inventors. In considering patent ability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly

owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 3, 4, 7, 8, 18 and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over JAMIN, Rev.fr.Gyncol.Obstet (1992), Vol. 87, No. 6, pp. 370-376 in view of MARTINDALE (1993), BAZIN et al., PARIS et al. and HODGEN (U.S .Pat. 5,552, 394)

MARTINDALE (1993) discloses that for administration by mouth, that oestradiol or oestradiol velerate are normally employed at doses of 1 to 2 mg daily and that oestradiol may also be used topically as transdermal skin patches to provide a systemic effect with patches available which release upto 100 micrograms of oestradiol daily (page 1191). It is disclosed that for equine conjugated oestrogens doses of 0.3 to 1.25 mg daily are given (page 1192). It is disclosed that combined oral contraceptive containing both an oestrogen and progestrogen in a fixed proportion are the most effective type for general use and taken for 21 days or occasionally 22 days followed by an interval of 7 or 6 days when menstrual bleeding will occur page (1177). It is disclosed that combined oral contraceptives appear to act by suppressing the mid-cycle peak of LH and FSH, thereby inhibiting ovulation and that both for estrogen and progestogen constitutents have this property (page 1177).

BENZIN et. al. disclose that doses of 1.25, 2.5 and 5 mg/day of nomegestrol acetate are effective in inhibiting ovulation and that doses of 2.5 and 5 mg/day results in very low oestradiol levels (page 1202)

PARIS et. al discloses that nomegestrol has no side effects such as androgenic activity (page 710, summary).

HODGEN discloses the combination of estrogen and progestin for 23-25 consecutive days of a 28 day cycle, preferably 24 days using tables containing both the estrogn and progestin and then for 4 days with placebo which is disclosed to be effective for contraception (Column 3, lines 50-61, column 3, lines 44-50). It is disclosed that useable estrogens include esters of estradiol, such as valerate, and conjugated equine estrogen (Column 4, lines 13-16). It is disclosed that different estrogens and progestins can be employed and that correlations in potency between the various estrogens and progestins are known (Column 4, lines 1-23).

The prior art discloses the combination of 5 mg/day nomegestrol acetate and 50 micrograms/day transdermal estradiol administered for 20 days of 28 day cycle. The difference between the prior art and the claimed invention is that the prior art does not expressly disclose the combination of nomegestrol ad estradiol in a single oral composition in the claimed range amounts. However, the prior art amply suggests the prior art discloses that

oral contraceptives and use of the same are well known including combination of estrogen and progestogen and cycles of administration, such as 20, 21, 22, 23-25 days, that nomegestrol acetate at doses falling within the claimed amounts result in very low estradiol levels and the prior art discloses equivalent dosages for estrogens including dosages of oral estradiol, esters thereof and conjugated estrogens that fall within the claimed ranges. As such, it would have been well within the skill of and one of ordinary skill in the art would have been motivated to combine nomegesterol and estradiol in a single oral dose for purposes of convenience, i.e. the patient would only have to remember to take a single dosage form a day as opposed to having to renmember to self-administer two dosage forms and would be motivated to vary doses and periods of administration depending on effectiveness in reducing the risk of pregnancy and avoiding low estradiol levels due to the nomegestrol. Further, one of the ordinary skill in the art would expect that any pharmaceutically acceptable form of estradiol could be used with the expectation that combination of the same with nomegestrerol would be effective in contraception.

In the case where the claimed ranges "overlap or lie inside ranges disclosed by the prior art" a prima facie case of obviousness exists. In re Wertheim, 541 F.2d 257, 191 USPQ 90 (CCPA 1976); In re Woodruff, 919 F.2d 1575, 16 USPQ2d 1934 (Fed. Cir. 1990) (The prior art taught carbon monoxide concentrations of "about 1-5%" while the claim was limited to "more than 5%". The court held that "about 1-5% allowed the concentrations slightly above 5% thus the ranges overlapped); In re Geisler, 116F.2d 1465, 1469-71, 43 USPQ2d 1362, 1365-66 (Fed. Cir. 1997) (Claim reciting thickness of a protective layer as falling within a range of "50 to 100 Angstroms" considered prima facie obvious in view of prior art reference teaching that "for suitable protection, the thickness of the protective layer should be not less than about 10 mm [i.e. 100 Angstroms]." The court stated that "by stating that suitable protection' is provided if the protective layer is about' 100 Angstroms thick, [the prior art reference] directly teaches the one of a thickness within [applicant's] claimed range."). Similarly, a prima facie case of obviousness exists where the claimed ranges and prior art ranges do not overlap but are close enough that one skilled in the art would have expected them to have the same properties.

Titanium Metals Corp of America v. Bannner, 778 F.2d 775, 227 USPQ 773 (Fed. Cir. 1985) Court held as proper a rejection of a claim directed to an alloy of 'having 0.8% nickel, 03% molybdenum, up to 0.1% iron, balance titanium" as obvious over reference disclosing g alloys of 0.75% nickel, 0.25% molybdenum, balance titanium and o.94% nickel, 0.31% molybdenum, balance titanium), "[A} prior art reference that discloses a range encompassing a somewhat narrower claimed range is sufficient to establish a prima facie case of obviousness." In re Peterson, 315 Fed 1325, 1330, 65 USPQ2d 1379, 1382-83 (Fed. Cir. 2003). Further, a range can be disclosed in multiple prior art references instead of in a single prior art reference. See Iron Grip Barbell Co., Inc. v USA SPORTS, IN., 392 F.3D 1317, 1322, 73 USPQ2d 1225, 1228 (Fed. Cir. 2004).

The rationale to modify or combine the prior art does not have to be expressly stated in the prior art; the rationale may be expressly or impliedly contained in the prior art or it may be reasoned from knowledge generally available to one of ordinary skill in the art, established scientific principles, or legal precedent established by prior case law. In re Fine, 837 F2d 1071, 5 USPQ2d 1596 (Fed. Cir 1988); In re Jones, 958 f.2dd 347, 21 USOQ2D

1313, 1317 (Fed. Cir. 1992). See also In re Kotzab, 217 F.3d 1365, 1370, 55
USPQ2d 1313, 1317 (Fed Cir. 2000)(setting forth test for implicit teachings); In re Eli Lilly & Co., 902 F.2d 943, 14 USPQ2d 1741 (Fed. Cir. 1990), (discussion of reliance on legal precedent); In re Nilssen, 851 F.2d 1401, 1403m 7 USPQ2d 1500, 1502 (Fed. Cir. 1988) (reference do not have to explicitly suggest combining teachings); and Ex parte Levengood, 28 USPQ2d 1300 (Bd. Pat. App. & Inter. 1993)(reliance on logic and should have, scientific reasoning).

In view of the above, the following may be concluded from the teachings of the prior art. The prior art discloses the combination of estrogens and progestogens in oral contraceptives, such as tablets, and that the equivalent dosages and dosage forms for estrogens and progestogens are known. The prior art discloses dose of nomegetrol acetate of 2.5 mg-5 mg/day, estradiol or estradiol valerate at 1-2 mg/day or equine conjugated estrogen at o.3 to 1.25 mg daily and trandsderman estradiol at doses of 50 mg and up to 100 neg. The prior art discloses administration of estrogens and progestogens in cycles of 20, 21, 22, 23-25

days per 28 days. The prior art discloses that nomegestrol acetate at said dosage levels results in very low levels of estradiol and that very low levels of estradiol can cause problems. The prior art also discloses that the equivalent dosages and dosage forms for estrogens and progestogens are known. The prior art discloses the combination of 5 mg/day of nomegestrol acetate and 50 mg/day transdermal estradiol in cycle of 20 days/28 days for contraception which avoids the problems caused by progestogen only formulations. As such, in view of the above, one of ordinary skill in the art would have been motivated to combine nomegestrol acetate at a dosage of 2.5 mg-5 mg/day with oral estradiol, ester thereof, such as valerate (1-2 mg/day) or equine conjugated estrogen (0.3 to 1.25 mg/day) with the expectation that the oral form of estradiol or equine conjugated estrogen at said dosages would comparable to the transdermal estradiolin avoiding the problems of low estradiol levels due to administration nomegestrol acetate and that a cycle of 20, 21, 22, 23-25 days/28 days would be effective in blocking pregnancies. Since dthe amounts and days disclosed in the prior art fall within, overlap or near that claimed, the ranges and amounts claimed are prima facie obvious in view of the prior art.

The consideration that amount of estradiol in JAMIN would not contribute to the contraceptive effect, however, Applicant provides no evidence of the same. Further, the prior art discloses that suppression of LH and FSH peaks is a function of both the estrogen and progestogen components of a combined oral contraceptive. As such, potentiation of the antiovulatory activity of nomegestrol by estradiol or its derivatives is not unexpected and the declaration of inventor Thomas does not appear to show unexpected activity. In any case, the ratio difference between JAMIN and the claimed invention is obviously the result of the use of transdermal estradiol in JAMIN. When comparable amounts of oral estrogens, such as estradiol at 1-2 mg, are substituted there is no patentably distinguishable difference between the prior art ratos and the ratio of at most 7.5 argued by Applicant. The fact that JAMIN does not disclose the dosage of 1.5-3.75 of nomegestrol or 0.5-3 mg of oral esradiol is not sufficient to overcome the rejection as the rejection is based on a combination of references. Further, there is no requirement that Jamin disclose a motivation to substitute oral administration for transdermal administration or disclose a motivation to administer the contraceptive specifically for 21-25 days.

The bases on MARTINDALE (1993) and HODGEN comparable and equivalent dosage forms for estradiol are well known in the art. As such, it would be well within the skill of one of ordinary skill in the art to substitute the transdermal estradiol with comparable amounts oral estradiol (which amounts, as indicated above, fall within the claimed ranges) with the expectation that the amounts of oral estradiol would potentiate the contraceptive activity of nomegestrol and inhibit any symptoms of low estradiol levels caused by the administration of the nomegestrol. To the extent that Applicant may argue that as background art, Powers et al. teaches away from the use of oral estradiol, in view of the wide use of oral contraceptives as indicated MARTINDALE (1993) above, any differences between oral estradiol and transdermal estradiol do not constitute a teaching away from the use of oral estradiol. "A known or obvious composition does not become patentable simply because it has been described as somewhat inferior to some other product for same use. " In Gurley, 27 F.3d 551, 554, 31 USPQ2d 1130, 1132 (Fed. Cir. 1994).

Claim Rejections - 35 USC § 103—2nd Rejection

Claims 3, 4, 7, 8, 18, 31 are rejected under 35 U.S.C. 103(a) as obvious over PLUNKETT et al. (US Re. 36,247) and BLANC et al. (Clinical Therapeutics, 1998), 20(5), 901-912). Both the references teach the art, which embraces instantly, claimed invention. See the entire documents, especially cited below.

1. Determining the scope and contents of the prior art.

PLUNKETT teaches a method of hormonal treatment for menopausal disorders involving continuous administration of progestagens and estrogens. See the entire document especially lines 40-51, col. 2; lines 63-67, col. 2; lines 1-67, col. 3; lines 18-25, and lines 1-5, col. 4; lines 46-50, col. 6.

The reference teaches continuous and uninterrupted administration of progestagen and estrogen. The actual unit dosage are selected according to conventionally known methods, e.g. body weight of patient and biological activity of hormones with the ultimate goal of producing the desired result

with minimum quantities of hormones. It does not disclose specifically nomegesterol acetate.

BLANC et al teaches continuous hormone replacement therapy combining nomegesterol acetate and gel, patch or oral estrogen. See the abstract of the invention; cols 1 and 2 on page 903col. 2 on page 904, Table 1 on page 905, Figure on page 906 ; Table II on page 907. Prior art also teach that bleeding occurs when treatment is discontinued.

2. Ascertaining the differences between the prior art and the claims at issue.

Instant claims are drawn to a method of treating deficiencies of estrogen by continuously administering a combination of estrogen and nomagesterol acetate. BLANC et al. teach the same combination, the ranges of the amounts overlap with the prior art teaching. Prior art teaches estradiol, 2 mg/dose whereas presently claimed amount is 0.3-3 mg and nomegesterol 2.5 mg/d whereas presently claimed amount 0.3 to 1.25 mg. The PLUNKETT et al differs from the instant invention in that it does not specifically name nomegesterol acetate.

3. Resolving the level of ordinary skill in the pertinent art.

It would be obvious to one skilled in the art at the time of invention to prepare a composition of NOMAC and estrogen to administer continuously combination of estrogen and nomegesterol as cited above.

4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Motivation is to use estrogen and progestagen continuously as taught by PLUNKETT et al. and use nomegesterol as progestagen because it gives in all patients' regular, progestagen-induced withdrawal bleed each month; and histological, ultra structural and biochemical changes were induced within the endometrium by all doses (0.5 mg, 1.0 mg; and 2.5 mg) is a potent progestogen. Blanc et al. teach same combination as combination of nomegestrol and estradiol. Thus, there has been ample motivation provided by the teachings of both the references cited above to prepare the instant invention in absence of any criticality or unexpected results.

There is motivation provided by the prior art to select NOMAC because at high doses there is no bleeding pattern and have different effect on endometrium.

Examiner notes, paragraph after Table 3 on page 4 of the declaration that applicant has cited the advantages which are known in the art.

In the light of the forgoing discussion, the Examiner's ultimate legal conclusion is that the subject matter defined by the instant claims would have been obvious within the meaning of 35 U.S.C. 103(a).

Response to Remarks and Declaration

Applicants arguments have been fully considered but was not found persuasive therefore rejections are maintained for the reasons cited above.

Double Patenting rejection over US 6,831,073 is maintained because the invention is inherently taught by the reference. The combination and dosage overlap therefore the property adherent to the amounts and dosage of the components are considered inherent.

Advantages of NOMAC was known at the time the invention filed

Obviousness rejection is maintained because at the time the invention was filed one skilled in the art would have been able to make the combination with the expectation to get better results because it was known at that NOMAC is not comparable to other progestins. Furthermore, **it was known at the time the invention was filed that contrary to 19 nor testosterone derivatives, it does not contain any estrogenic and androgenic residual activity and also contrary to 17alpha-hydroxyprogesterone derivatives, it has a strong antigonadotropic activity. The citation of NOMAC brings original properties and comparison of table 1 (page 2) is not Applicants work. It was already known at the time when the invention was filed. The declaration should contain only the work done by the Applicants and proper comparison. Applicant should not confuse their work with already known in the art without mentioning the source. Furthermore, in the declaration Applicant also cite WO 95/17194 and EP 025607 and Plummet's patent which is not relevant to the present claims.**

Declaration further cites on page 4 that progestins continuously given with an estrogen induce an endometrial atrophy. Example 1 and 2 on page 6 of the declaration has been considered however, the art known at that time about advantages of NOMAC the combination of NOMAC and estradiol at the time the invention was filed would have been obvious. The present specification states

that when the hormonal combination is given for a contraceptive purpose, the aim of the nomegestrol acetate is to stop ovulation and the aim of the estrogenic compound is to compensate for hypoestrogenia and ensure a better control of the cycle (Specification, page 7, lines 20-30). As such, the Specification does not disclose continuous administration with respect to achieving contraception; only cyclic administration by daily administering the composition from 21 to 25 days per month or 21 to 28 days, starting on the first day of the menstrual cycle (specification, page 7, lines 1-5, Page 11, lines 4-7). Claims 1-10 do not indicate cyclic administration by daily orally administering the hormonal product for 21 to 25 days per month and claim 34 does not indicate the same or daily administration for 21 to 28 days, starting on the first day of the menstrual cycle. **The declaration does not overcome these issues**

MARITINADALE (1993) and HODGEN comparable and equivalent dosage forms for estradiol are well known in the art. As such, it would be well within the skill of one of ordinary skill in the art to substitute the transdermal estradiol with comparable amounts oral estradiol (which amounts, as indicated above, fall within the claimed ranges) with the expectation that the amounts of oral estradiol would potentiate the contraceptive activity of nomegestrol and inhibit any symptoms of low

estradiol levels caused by the administration of the nomegestrol. To the extent that Applicant may argue that as background art, Powers et al. teaches away from the use of oral estradiol, in view of the wide use of oral contraceptives as indicated Martindale (1993) above, any differences between oral estradiol and transdermal estradiol do not constitute a teaching away from the use of oral estradiol. "A known or obvious composition does not become patentable simply because it has been described as somewhat inferior to some other product for the same use." In re Gurley, 27 F.3d 551,554, 31 USPQ2d 1130, 1132 (Fed. Cir. 1994).

> Applicant argues that Bazin et al. teaches away from the claimed invention because the dose of 1.25 mg/day ofnomegestrol acetate increased oestradiol concentration. However, said dosage is outside the claimed minimum dosage of 1.5 mg/day and, as indicated above, the dosages of 2.5 mg and 5 mg/day result in very low levels of oestradiol. As such, Bazin et al. does not teach away from adding estradiol to formulate a product in combination with nomegestrol acetate at the dosages of nomegestrol acetate claimed.
>
> Applicant argues extensively as to what Paris et al. does not disclose, As indicated above, in a rejection based on a combination of references there is no requirement that Paris et al. disclose each and

every element of the claimed invention. Obviousness does not require absolute predictability, as such; the fact that the tests were performed on rodents does not overcome the rejection. Applicant has not provided any evidence that one of ordinary skill in the art may not rely on tests performed on animals is said reference to predict or suggest the activity of the progestogen in women.

HODGEN is not required to disclose the use of nomegestrol acetate. However, there is ample motivation and incentive to use alternative progestogens as HODGEN itself discloses that alternative progestogens can be used in place of the specifically disclosed progestogen. Disclosed examples and preferred embodiments do not constitute a teaching away from a broader disclosure or nonpreferred embodiments. In re Susi, 440 F.2d 442, 169 USPQ 423 (CCPA 1971).

Therefore, the claimed invention, as a whole, would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, because every element of the invention has been collectively taught by the combined teachings of the references.

Examiner concludes that claims and specification does not provide any new concept or invention for the reasons cited above. To emphasize this point Examiner would like to refer to Applicants to Genetech, 108 F.3d at 1366 and Brenner 383 U.S. 519, 536, 148 USPQ 689, 696 (1966)" which states that "a patent is not a hunting license. It is not a reward for research, but a compensation for its successful conclusion" and "patent protection is granted in return for an enabling disclosure of an invention, not for vague limitations of general ideas that may or may not be workable."

One cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller,* 642 F,2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Further the test for obviousness is not whether the features of secondary reference may bodily incorporated into the structure of the primary reference, nor is it that the claimed invention must be expressly suggested in any one or all of the references. Rather, the test is what the combined teaching of the references would have been suggested to those of ordinary skill in the art. See *In re Keller*, 642 F 2d 413, 208USPQ 871 9CCPA 1981).

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Communication

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sabiha Qazi whose telephone number is (571) 272-0622. The examiner can normally be reached on any business day except Wednesday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Krass Frederick can be reached on (571) 272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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/Sabiha Qazi/
Primary Examiner, Art Unit 1612